

Claims

1. A method for identifying a nematode having enhanced susceptibility to a pathogen, said method comprising the steps of:

- 5 (a) exposing a mutagenized nematode to a pathogen; and
(b) determining survival of said mutagenized nematode when exposed to said pathogen, decreased survival of said mutagenized nematode relative to a non-mutagenized nematode identifying said mutagenized nematode as one having enhanced susceptibility to the pathogen.

10 2. The method of claim 1, wherein said mutagenized nematode is *C. elegans*.

3. The method of claim 2, wherein said *C. elegans* is an N2 L4 worm.

15 4. The method of claim 1, wherein said pathogen is a bacterium.

5. The method of claim 4, wherein said bacterium is *Pseudomonas aeruginosa* (strain PA14).

20 6. The method of claim 4, wherein said bacterium is *Enterococcus faecalis*.

7. The method of claim 1, wherein said mutagenized nematode is exposed to said pathogen under slow killing conditions.

25 8. The method of claim 1, wherein said mutagenized nematode comprises a mutation in a component of a MAPK signal transduction pathway.

9. The method of claim 8, wherein said component of the MAPK signal transduction pathway is *esp-2*.

30 10. The method of claim 8, wherein said component of the MAPK signal transduction pathway is *esp-8*.

11. The method of claim 8, wherein said component of the MAPK signal transduction pathway is *pmk-1*.

12. A method for identifying a pathogen defense response gene, said method comprising the steps of:

- (a) exposing a mutagenized nematode to a pathogen;
- (b) determining survival of said mutagenized nematode when exposed to said pathogen, decreased survival of said mutagenized nematode relative to a non-mutagenized nematode indicating a mutation in a nematode pathogen defense response gene; and
- (c) using said mutation as a marker for identifying said pathogen defense response gene.

13. The method of claim 12, wherein said mutagenized nematode is *C. elegans*.

14. The method of claim 13, wherein said *C. elegans* is an N2 L4 worm.

15. The method of claim 12, wherein said pathogen is a bacterium.

16. The method of claim 15, wherein said bacterium is *Pseudomonas aeruginosa* (strain PA14).

17. The method of claim 15, wherein said bacterium is *Enterococcus faecalis*.

18. The method of claim 12, wherein said mutagenized nematode is exposed to said pathogen under slow killing conditions.

19. The method of claim 12, wherein said mutagenized nematode pathogen response gene comprises a mutation in a component of a MAPK signal transduction pathway.

20. The method of claim 19, wherein said component of the MAPK signal transduction pathway is *esp-2*.

21. The method of claim 19, wherein said component of the MAPK signal transduction pathway is *esp-8*.

22. The method of claim 19, wherein said component of the MAPK signal transduction pathway is *pmk-1*.

23. A method for identifying a nematode having enhanced susceptibility to a pathogen, said method comprising the steps of:

- (a) providing a nematode comprising a double-stranded RNA (dsRNA),
5 wherein said dsRNA silences the expression of an endogenous nematode gene;
- (b) exposing said nematode to a pathogen; and
- (c) determining survival of said nematode when exposed to said pathogen,
10 decreased survival of said nematode having dsRNA relative to a control nematode identifying the nematode having dsRNA as one with enhanced susceptibility to the pathogen.

24. The method of claim 23, wherein said nematode is *C. elegans*.

25. The method of claim 24, wherein said *C. elegans* is an N2 L4 worm.

26. The method of claim 23, wherein said dsRNA is microinjected into said nematode.

27. The method of claim 23, wherein said nematode comprising said dsRNA is
20 a result of a nematode that ingests dsRNA-expressing bacteria.

28. The method of claim 23, wherein said pathogen is a bacterium.

29. The method of claim 28, wherein said bacterium is *Pseudomonas*
25 *aeruginosa* (strain PA14).

30. The method of claim 28, wherein said bacterium is *Enterococcus faecalis*.

31. The method of claim 23, wherein said nematode is exposed to said pathogen
30 under slow killing conditions.

32. The method of claim 23, wherein said silenced endogenous nematode gene comprises a component of a MAPK signal transduction pathway.

33. The method of claim 32, wherein said component of the MAPK signal
35 transduction pathway is *esp-2*.

34. The method of claim 32, wherein said component of the MAPK signal transduction pathway is *esp-8*.

35. The method of claim 32, wherein said component of the MAPK signal transduction pathway is *pmk-1*.

36. A method for identifying a pathogen defense response gene, said method comprising the steps of:

(a) providing a nematode comprising a dsRNA, wherein said dsRNA silences an endogenous nematode gene;

(b) exposing said nematode to a pathogen;

(c) determining survival of said nematode when exposed to said pathogen, wherein decreased survival of said nematode having dsRNA relative to a control nematode indicates that said dsRNA silences a pathogen defense gene; and

(d) determining the nucleic acid sequence said dsRNA, thereby identifying said pathogen defense response gene.

37. The method of claim 36, wherein the nucleic acid sequence of said dsRNA is known.

38. The method of claim 36, wherein said nematode is *C. elegans*.

39. The method of claim 38, wherein said *C. elegans* is an N2 L4 worm.

40. The method of claim 36, wherein said dsRNA is microinjected into said nematode.

41. The method of claim 36, wherein said nematode comprising said dsRNA is a result of a nematode that ingests dsRNA-expressing bacteria.

42. The method of claim 36 wherein said pathogen is a bacterium.

43. The method of claim 39, wherein said bacterium is *Pseudomonas aeruginosa* (strain PA14).

44. The method of claim 39, wherein said bacterium is *Enterococcus faecalis*.

45. The method of claim 36, wherein said nematode is exposed to said pathogen under slow killing conditions.

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46. The method of claim 36, wherein said silenced pathogen defense gene comprises a component of a MAPK signal transduction pathway.

47. The method of claim 46, wherein said component of the MAPK signal transduction pathway is *esp-2*.

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48. The method of claim 46, wherein said component of the MAPK signal transduction pathway is *esp-8*.

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49. The method of claim 46 wherein said component of the MAPK signal transduction pathway is *pmk-1*.

50. A method for identifying a compound that enhances a defense response to a pathogen, said method comprising the steps of:

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(a) exposing a nematode, having enhanced pathogen susceptibility, to a test compound and a pathogen; and

(b) determining survival of said nematode exposed to said pathogen, increased survival of said nematode relative to the survival of said nematode in the absence of said test compound identifying a compound that enhances a defense response to a pathogen.

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51. The method of claim 50, wherein said nematode is a nematode identified according to the method of claim 1.

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52. The method of claim 50, wherein said nematode is a nematode identified according to the method of claim 23.

53. The method of claim 50, wherein said nematode is *C. elegans*.

54. The method of claim 53, wherein said *C. elegans* is an N2 L4 worm.

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55. The method of claim 50, wherein said pathogen is a bacterium.

56. The method of claim 55, wherein said bacterium is *Pseudomonas aeruginosa* (strain PA14).

5 57. The method of claim 55, wherein said bacterium is *Enterococcus faecalis*.

58. The method of claim 50, wherein said nematode is exposed to said pathogen under slow killing conditions.

10 59. The method of claim 50, wherein said test compound is provided in a compound library.

60. The method of claim 50, wherein said test compound is a small organic compound.

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61. The method of claim 50, wherein said test compound is a peptide, peptidomimetic, or an antibody or fragment thereof.

20 62. The method of claim 50, wherein said mutagenized nematode comprises a mutation in a component of a MAPK signal transduction pathway.

63. The method of claim 62, wherein said component of the MAPK signal transduction pathway is *esp-2*.

25 64. The method of claim 62, wherein said component of the MAPK signal transduction pathway is *esp-8*.

65. The method of claim 62, wherein said component of the MAPK signal transduction pathway is *pmk-1*.

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66. A method for identifying a component of a MAPK signal transduction pathway conferring innate immunity to a nematode, said method comprising the steps of:

(a) providing a nematode having a mutation in a component of a MAPK signal transduction pathway and a pathogen; and

35 (b) determining survival of said nematode when exposed to said pathogen, decreased survival of said nematode relative to a wild type nematode identifying a

component of said MAPK signal transduction pathway that confers innate immunity to a nematode.

67. The method of claim 66, wherein said component of the MAPK signal
5 transduction pathway is a gene encoding a MAPK.

68. The method of claim 67, wherein said gene encoding the MAPK is *pmk-1*.

69. The method of claim 66, wherein said component of the MAPK signal
10 transduction pathway is a gene encoding a MAPKK.

70. The method of claim 66, wherein said gene encoding the MAPKK is *esp-2*.

71. The method of claim 66, wherein said component of the MAPK signal
15 transduction pathway is a gene encoding a MAPKKK.

72. The method of claim 66, wherein said MAPKKK is *esp-8*.

73. A method for identifying a nematode having enhanced susceptibility to a
20 pathogen, said method comprising the steps of:

(a) providing a nematode comprising a double-stranded RNA (dsRNA),
wherein said dsRNA silences the expression of a component of a MAPK signal
transduction pathway;

(b) exposing said nematode to a pathogen; and

25 (c) determining survival of said nematode when exposed to said pathogen,
decreased survival of said nematode having dsRNA relative to a control nematode
identifying the nematode having dsRNA as one with enhanced susceptibility to the
pathogen.

74. The method of claim 73, wherein said component of the MAPK signal
30 transduction pathway is a gene encoding a MAPK.

75. The method of claim 74, wherein said gene encoding the MAPK is *pmk-1*.

76. The method of claim 73, wherein said component of a MAPK signal
35 transduction pathway is a gene encoding a MAPKK.

77. The method of claim 76, wherein said gene encoding the MAPKK is *esp-2*.

78. The method of claim 73, wherein said component of a MAPK signal
5 transduction pathway is a gene encoding a MAPKKK.

79. The method of claim 78, wherein said gene encoding the MAPKKK is
esp-8.

10 80. A method for identifying a compound that enhances a defense response to a
pathogen, said method comprising the steps of:

(a) exposing a nematode, having a mutated MAPK signaling pathway, to a test
compound and a pathogen; and

(b) determining survival of said nematode exposed to said pathogen, increased
15 survival of said nematode relative to the survival of said nematode in the absence of said
test compound identifying a compound that enhances a defense response to a pathogen.

81. The method of claim 80, wherein said component of the MAPK signal
transduction pathway is a gene encoding a MAPK.

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82. The method of claim 81, wherein said gene encoding the MAPK is *pmk-1*.

83. The method of claim 80, wherein said component of the MAPK signal
transduction pathway is a MAPKK.

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84. The method of claim 83, wherein said gene encoding the MAPKK is *esp-2*.

85. The method of claim 80 wherein said component of the MAPK signal
transduction pathway is a MAPKKK.

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86. The method of claim 85, wherein said gene encoding the MAPKKK is
esp-8.